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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/611,257	07/06/2000	Terrance P. Snutch	381092000721	5449

25225 7590 05/11/2005

MORRISON & FOERSTER LLP
3811 VALLEY CENTRE DRIVE
SUITE 500
SAN DIEGO, CA 92130-2332

EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/611,257	SNUTCH ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2;4-6,14 and 18-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,14,18-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7 April 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks and amendments filed 28 March 2005 have been entered. Claims 1, 6, 14, and 18 have been amended. Applicant has added new claims 19 – 26. Claims 1, 2, 4 – 6, 14, and 18 – 26 are pending.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Information Disclosure Statement

3. The information disclosure statement filed 7 April 2005 has been considered by the examiner, PTO-1449 is attached.

Withdrawn Objections and Rejections

4. The following objections and rejections are hereby withdrawn:

The rejection of claim 6 under 35 USC 112, second paragraph. Applicant has amended the claim as suggested by the examiner.

The rejection of claim 2 under 35 USC 112, first paragraph, for failing to meet the written description requirement. Applicant has amended the claim to recite 100% identity to SEQ ID NO:37.

The rejection of claims 1, 4 – 6, and 14 under 35 USC 102(e). Applicant has amended the claims, they are now limited to nucleic acid sequences encoding polypeptides at least 99% identical to SEQ ID NO:24 or 100% identical to SEQ ID NO:37.

Rejections Maintained

5. Claims 1, 2, 4 – 6, 14, and 18 – 26 stand rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

On p. 5 of the remarks filed 28 March 2005 applicant asserts that the claimed nucleic acids are useful to produce alpha-1G calcium channel subunits, which are themselves useful to screen for modulators which would be expected to be useful for disorders where undesirable T-type calcium channel activity is present, including "epilepsy, sleep disorders, mood disorders, cardiac hypertrophy and arrhythmia and hypertension among others." This is not a specific and

substantial utility for the reasons made of record in the office action mailed 21 December 2004 and reiterated herein.

Applicant refers the examiner's attention to U.S. Patent 6,358,706, which discloses a closely related sequence. Applicant asserts, on p. 5 of the remarks, that the utility of the '706 patent is the same as claimed in the instant application, and refers specifically to column 17, line 17 as containing a list of conditions that can be treated. First of all, applicant's reference to the '706 patent as establishing a patentable utility for the claimed nucleic acid is not persuasive because each application is examined on its own merits. In the decision of *In re Hutchinson*, 69 USPQ 138 (CCPA, 1946), the court held that:

> "We are not concerned, of course, with the allowed claims in either the patent or in this application. The sole question for our determination is whether the six article claims on appeal were properly rejected below, and this we pass upon without further reference to, and without comparing them with, the claims in the patent or the claims which stand allowed in this application."

In essence, the position in the instant application that each application is examined on its own merits can be found in the judicial precedent cited above. The rejections in the instant application will only be withdrawn if they are shown to be legally or factually unsound.

It is acknowledged that the list of conditions provided in the '706 patent includes those listed by applicant. However, the '706 patent does not assert that those diseases can in fact be treated with modulators identified in screening assays. The first sentence of the paragraph beginning at column 17, line 17 states "Modulators identified in the assays disclosed herein are useful *candidates* as therapeutic agents for the treatment disorders that are mediated by human alpha1G-c activity. [emphasis added]" Neither the instant specification nor the art of record (i.e. the '706 patent) indicates that modulators identified in screening assays are in fact useful as therapeutics. Applicant has not established a nexus between any of the diseases listed and undesirable T-type calcium channel activity, and the '706 patent merely asserts that any modulators identified are useful as candidates. However any molecule is useful as a "candidate", since the term does not require that the molecules have any efficacy whatsoever.

Furthermore the list of diseases provided by applicant is exemplary, not limited. Applicant has asserted that the claimed nucleic acids are useful for screening assays in diseases other than those listed, and has not established a nexus between any disease, listed or not, and the instantly claimed nucleic acids or the proteins they encode.

Applicant refers to the decisions in *Bayer*, *Sibia*, and *University of Rochester* as providing support for the utility of the instantly claimed nucleic acids. It is not immediately apparent to the examiner why the *Bayer* case is relevant here. The legal issues in *Bayer* had to do with whether a patented process claim had been infringed by importation of a product that could reasonably have been identified through said process. While the subject matter was similar to the asserted utility in the instant case (i.e. identification of compounds), in the *Bayer* case, the court implicitly relied upon the assumption that all U.S. patents are valid on their face, as they have in fact passed through the rigors of examination. In the instant case, the examiner has rejected all claims under 35 U.S.C. § 101 and 112 because applicant has not established a nexus between the claimed invention and a specific disease, disorder, or physiological condition.

It is acknowledged that utility was not an issue in the *Sibia* case, and that the patent at issue in the *Sibia* (U.S. Patent 5,401,629) case was drawn to methods of identifying compounds that modulate cell surface protein-mediated activity, and that the patent asserted that the methods were useful for finding modulators of ion channel activity (see column 4, lines 36 – 40). In the instant application, the claims are drawn to nucleic acids, which applicant asserts are useful to identify modulators of ion channels. It appears applicant is relying on the fact that the court did not overturn the '629 patent based on a lack of utility as an argument for utility in the instant case. Applicant is again referred to the court's decision in *Hutchinson*, which stated that the each application is to be examined on its own merits.

In the *Rochester* case, the claims were drawn to methods of identifying compounds (see U.S. Patent 5,837,479). The claims were not deemed invalid as lacking utility. However, the *Rochester* case is different from the instant case in an important fashion. In the '479 patent, applicant had demonstrated a nexus between the claimed methods and a specific disease or condition. The specification of the '479 patent indicates that the cell lines are useful for identifying responses to nonsteroidal antinflammatory drugs (see column 44, lines 40 – 67). Clearly in the '479 patent there was a nexus between claimed methods and a specific condition, namely inflammation. In the instant case, there is not.

On p. 7 of the remarks, applicant argues that there are dozens of patents issued directed to methods of screening compounds that would be useful to treat particular conditions. Applicant is again reminded that the claims in issued patents are not relevant to the utility of the instantly claimed nucleic acid; each application is examined on its own merits. Applicant argues

at the end of p. 7 of the remarks that the asserted utility (i.e. use in screening assays to identify modulators which can then be used as treatments for diseases) is specific and substantial. Applicant's arguments have been fully considered but they are not persuasive.

MPEP § 2107.03 is particularly relevant to the discussion of asserted utilities of pharmacological agents and related methods. It is noted that proof of treatment in human subjects is not required for a substance to be useful. However, MPEP § 2107.03 (I) states that

> "As a general matter, evidence of pharmacological or other biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility. Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881 (CCPA 1980). An applicant can establish this reasonable correlation by relying on statistically relevant data documenting the activity of a compound or composition, arguments or reasoning, documentary evidence (e.g., articles in scientific journals), or any combination thereof."

Here, applicant asserts that the instantly claimed nucleic acids are useful in screening assays to identify agents that can be used in a non-limiting list of conditions with different mechanisms and etiologies. Applicant has not presented statistically relevant data documenting the activity of a compound, or documentary evidence establishing a nexus between the claimed nucleic acids and a specific disease, or convincing arguments or reasoning.

On p. 7 of the remarks, applicant refers the examiner to Example 12 of the Utility Guidelines, which are based on claims to a receptor. Applicant argues that in that example, utility is lacking only because there is not a connection between the receptor and a specific disease. In the instant case, applicant has also failed to disclose a nexus between any of the diseases and conditions listed on p. 5 of the specification and the instantly claimed nucleic acids. There is no indication that expression of the nucleic acids or their encoded proteins, or the activity of those proteins are different in any of those conditions. Finally, applicant has admitted on the record (remarks, p. 5, final paragraph) that compounds which are useful in treating the diseases still have not yet actually been identified by the methods for which the claimed nucleic acids are allegedly useful. Clearly significant further research is necessary to use the invention as claimed. The rejection of claims 1, 2, 4 – 6, 14, and 18 is maintained for the reasons made of record previously and explained in further detail above. New claims 19 – 26 stand rejected for the same reasons.

6. Claims 1, 2, 4 – 6, 14, and 18 – 26 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and

substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

7. Claims 1, 4 – 6, and 14 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the previous office action the examiner stated that the claims are drawn to a genus of sequences which had not been described. Applicant has amended the claims to recite 100% identity to SEQ ID NO:37 and either 99% or 100% identity to SEQ ID NO:24. Claims which recite 100% identity meet the written description requirement. Claims drawn to 99% identity still fail to meet the written description requirement. Applicant has not disclosed any nucleic acid sequences which encode polypeptides less than 100% identical to either SEQ ID NO:24 or 37. In the remarks filed 28 March 2005, applicant indicates that the claims have been amended to recite 100% identity to SEQ ID NO:37 but has not addressed the issue of sequences that are less than 100% identical to the disclosed sequences.

Priority

8. In the previous office action the examiner stated that since the instant application does not meet the requirements of 35 USC 112, first paragraph, it is not entitled to priority of earlier-filed applications, including 09/346794. In the remarks filed 28 March 2005, applicant argues that the utility and enablement requirements have been met and therefore priority should be granted. For the reasons made of record and detailed above, the utility and enablement rejections stand and therefore priority to earlier applications is denied. The priority date for this application is the filing date, 7/6/2000.

New Rejections

Claim Rejections - 35 USC §§ 102 and 103

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1 and 14 rejected are under 35 U.S.C. 102(b) as being anticipated by GenBank locus AF027984 and Perez-Reyes et al. (1998. Nature 391:896-900, cited on applicant's information disclosure statement filed 15 March 2001), as evidenced by Promega catalog pSP72. Applicant is advised that these refer to the same sequence; GenBank AF027984 identifies Perez-Reyes et al. as the publication corresponding to this sequence, and Perez-Reyes et al. indicate the same information in the final paragraph of the Acknowledgements section on p. 900.

Perez-Reyes et al. teach the isolation of nucleic acid encoding the rat alpha-1G T-type calcium channel, which is AF027984. The nucleic acid taught by Perez-Reyes encodes a polypeptide 99.78% identical to applicant's SEQ ID NO:24, meeting the limitation of claim 14. Perez-Reyes et al. also teach inserting said sequence into the pSP72 vector (see p. 899, first column, last sentence of the section entitled cDNA Library Screening). Promega catalog indicates that this vector includes sequences for expression controlled by either T7 or SP6 polymerases, meeting the limitation of claim 1, which is drawn to the same nucleic acid as claim 14 (i.e. encoding a polypeptide at least 99% identical to SEQ ID NO:24) operably linked to control sequences to effect its expression. A skilled artisan would at once realize that the T7 and SP6 control sequences taught by Promega catalog are sequences which are used to control expression.

11. Claims 4 – 6 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Perez-Reyes et al., in view of Brizzard et al. (1997.

Current Protocols in Neuroscience 5.8.1 – 5.8.10). Perez-Reyes et al. teach expression cassettes comprising a sequence encoding a polypeptide 99.78% identical to SEQ ID NO:24, as detailed in the previous paragraph. Perez-Reyes also teach host cells (*Xenopus* oocytes and mouse NIE-115 neuroblastoma cells) modified to contain the DNA expressing an alpha-1G channel (see p. 899, second column, as well as p. 898, Figure 3 and the text above it). Perez-Reyes et al. teach the cloning of mouse, rat, and human alpha-1G channels, and it is not clear from the text which species' DNA was used in the experiments involving *Xenopus* oocytes. If the rat sequence was used, this is a rejection under 35 USC § 102 (b). The teachings of Perez-Reyes et al. meet the claim limitations because they teach recombinant host cells containing the instantly claimed nucleic acids, including mammalian cells (meeting the limitations of claims 4 and 5) as well as methods of expressing functional recombinant protein in said cells, meeting the limitations of claim 6.

If either mouse or human sequence was used, the teachings of Brizzard et al. become relevant. Brizzard et al. teach methods of epitope tagging of recombinant proteins, comprising making recombinant cells expressing said proteins, and indicate that this method is successful in *Xenopus* oocytes (p. 5.8.6, second column). Brizzard et al. teach that epitope tagging is useful for detection of proteins for which no antibodies exist. It would have been obvious to one of ordinary skill in the art to make recombinant *Xenopus* oocytes expressing the nucleic acid, as taught by Brizzard et al., with a reasonable expectation of success. A motivation would be to express epitope-tagged proteins for detection, as suggested by Brizzard.

12. Claims 1, 5, 6, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Perez-Reyes et al., in view of Brizzard et al. Perez-Reyes et al. teach isolated nucleic acids encoding protein 99.78% identical to SEQ ID NO:24, as detailed in the preceding paragraphs. Perez-Reyes et al. do not teach recombinant mammalian cells or methods of making recombinant protein.

Brizzard et al. teach methods of making recombinant protein by culturing COS cells. The methods are explained in detail on pp. 5.8.2 – 5.8.3. These methods are useful for detection of proteins, specifically epitope-tagged proteins. Brizzard et al. teach COS cells, which are mammalian cells, as a preferred embodiment, and indicate that the prior art has other methods of making recombinant mammalian cells for the same purpose (see p. 5.8.6, end of first column). It would have been obvious to one of ordinary skill in the art to make recombinant mammalian cells comprising the DNA of Perez-Reyes et al., and to make recombinant protein

from those cells. Both methods are taught by Brizzard, and Brizzard et al. further teach that these methods are useful in the purification of proteins without antibodies specific for those proteins. A motivation to combine these teachings would be to produce large amounts of purified protein, as suggested by Brizzard.

13. Claim 14 is rejected under 35 U.S.C. 102(b) as being anticipated by Stratagene random primers, 1991 catalog, p. 66.

Stratagene teaches the use of random 9-mers capable of hybridizing with all possible gene sequences. The random primers meet the claim limitations because the primers are a complement to polynucleotides that encoded both SEQ ID NOS:24 and 37. The claim language does not require that the nucleic acid be the full-length complement, only that it comprise one of the complements of an alpha-1G subunit. A skilled artisan would realize that there are many sequences which are complementary to at least a fragment of said subunit, and that a random9-mer would be included in such a broad definition. This rejection could be overcome by amending the claim to recite either "the complement" or "the full-length complement".

Conclusion

14. No claim is allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.
May 9, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
5-10-05